International Journal of Cardiology 166 (2013) 132–140

Contents lists available at SciVerse ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Navigating the mini-maze: Systematic review of the first results and progress of minimally-invasive surgery in the treatment of atrial fibrillation ☆

Sébastien P.J. Krul [a], Antoine H.G. Driessen [a,b], Aeilko H. Zwinderman [c], Wim J. van Boven [d], Arthur A.M. Wilde [a], Jacques M.T. de Bakker [a,e], Joris R. de Groot [a,*]

[a] Heart Failure Research Center, Department of Clinical and Experimental Cardiology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands
[b] Department of Cardiothoracic Surgery, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands
[c] Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands
[d] Department of Cardiothoracic Surgery, St. Antonius Hospital, Nieuwegein, The Netherlands
[e] Interuniversity Cardiology Institute of the Netherlands, Utrecht, The Netherlands

ARTICLE INFO

Article history:
Received 13 July 2011
Accepted 15 October 2011
Available online 9 November 2011

Keywords:
Ablation
Atrial fibrillation
Minimally-invasive surgery

ABSTRACT

Background: In this paper we present a systematic literature overview and analysis of the first results and progress made with minimally-invasive surgery using RF energy in the treatment of AF. The minimally-invasive treatment for atrial fibrillation (AF) tries to combine the success rate of surgical treatment with a less invasive approach to surgery. It has the additional potential advantage of ganglion plexus (GP) ablation and left atrial appendage exclusion. Furthermore, additional left atrial ablation lines (ALAL) can be created in non-paroxysmal AF patients.

Methods: For the search query multiple databases were used. Exclusion and inclusion criteria were applied to select the publications to be screened. All remaining articles were critically appraised and only relevant and valid articles were included in our results.

Results: Twenty-three studies were included. In 15 studies GPs around the pulmonary veins were ablated. In four studies ALAL were performed. Single procedure success rate was 69% (95% CI, range 58%–78%) without

Mortality was
% pulmonary,

Conclusions: Twenty-three studies of minimally-invasive surgery for AF have been reviewed with success rates between that of the standard maze procedure and catheter ablation. These first combined results show promise; however, minimally-invasive surgery is still evolving, for instance by the recent inclusion of electrophysiological endpoints. Furthermore, the type of ALAL and the additional value of GP ablation have to be elucidated.

1. Introduction

Treatment of AF, worldwide the most common supraventricular arrhythmia, is a challenge for the cardiologist, despite increasing pharmalogical and technological options. Some patients experience no or few complaints during AF while others are adequately managed with pharmacologic rate or rhythm control. Unfortunately, there is a group of patients with AF who have debilitating symptoms during AF that cannot sufficiently be treated with AAD. The Cox–Maze procedure described by Cox et al. was the first invasive surgical procedure for the treatment of AF [1,2]. It has a success rate of 75%–95% after up to 15 years of follow up. In 1998 Haïssageurre et al. published a landmark paper in which an endovascular approach was described to target pulmonary vein triggers [3]. Catheter based interventions have a lower single procedure success rate of 57% (95% CI, range 50%–64%) off AAD after a mean follow up of 14 months, but are less invasive than the Cox–Maze-III procedure, which requires open heart surgery. Indeed, a single procedure is not always enough to prevent AF recurrences and most patients require multiple procedures to achieve a success rate of 71% (95% CI, 65%–77%) off AAD [4]. In 2005 Wolf et al. described the first results of 21 patients treated with a minimally-invasive surgical approach to PVI [5]. The minimally-invasive procedure tries to combine the success rate of surgical treatment with a less invasive intervention for the patient akin to catheter ablation. Since the first publications, experience with the minimally-invasive procedure has increased, but the technique has not yet been established as a regular treatment option of AF. A potential advantage of the epicardial approach is the possibility of GP ablation, which may modulate the substrate for

Abbreviations: AAD, antiarrhythmic drugs; AF, atrial fibrillation; ALAL, additional left atrial lesion set; AT, atrial tachycardia; CI, confidence interval; GP, ganglionated plexus; LAA, left atrial appendage; LSP, long standing persistent; PVI, pulmonary vein isolation; RF, radiofrequency.

☆ Funding: 2009T021, Netherlands Heart Foundation, The Hague, Netherlands.

* Corresponding author at: Department of Cardiology, Academic Medical Centre, University of Amsterdam, Meibergdreef 9, 1100 DD Amsterdam, The Netherlands.
E-mail address: j.r.degroot@amc.uva.nl (J.R. de Groot).

0167-5273 © 2011 Elsevier Ireland Ltd. Open access under the Elsevier OA license.
doi:10.1016/j.ijcard.2011.10.011

AF-induction [6]. Furthermore, ALAL can be created to prevent AF recurrence and AT in patients requiring more extensive ablation. The risk of embolic events might be reduced through the possibility of excluding the LAA during surgery. Multiple energy sources have been investigated, including microwave [7–9] or high frequency ultrasound [10], but application of these energy sources results in a lower success rate than RF energy. In this paper we present an analysis of the first results and progress made with minimally-invasive surgery, using RF energy only, in the treatment of AF. Additionally we discuss the recent developments and the place of minimally-invasive surgery in the therapeutic options of AF-treatment.

2. Methods

2.1. Search query

For the search query the following databases were used; Pubmed and Embase on 07/07/2011. The search query is shown in Table 1. We have added the results of Pison et al. (Pison et al., submitted) to the analysis.

2.2. Search strategy

The exclusion criteria were chosen to make a selection based on title and/or abstract, hereby selecting the papers needed to screen. Inclusion criteria were applied on the full text of the selected articles. Exclusion and inclusion criteria are listed in Table 1. Studies using RF-energy were selected as this method of ablations shows superior results compared with other energy sources like high intensity focused ultrasound [10] and microwave ablation [7–9]. Doubles were filtered manually and all remaining articles were combined. All included full texts were screened on references.

2.3. Statistical analysis

Forest-plots to present an overview of the studies have been made using Meta-Analyst Beta 3.13 (Tufts Medical Center, Boston, MA) [11]. No individual patient data were available to perform a meta-analysis; however an overall freedom of AF curve was made to show the results of all studies. A freedom from AF analysis curve was chosen to estimate the combined effect of the different studies based on the reported proportions of success and number of patients. The analysis was performed with the Statistical Package for the Social Sciences, version 15.0 for Windows XP (SPSS, Chicago, IL, USA). The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

3. Results

A total of 24 studies were found using our search query in Embase of whom 22 were also found in Pubmed [5,12–31]. Two studies on ≤10 patients were excluded [32,33]. An overview of the remaining 22 studies and the study of Pison et al. is presented in Table 2. All studies were observational in nature and 18/23 studies were performed in a single centre [5,13–18,20–23,26,27,29–31,34]. In total there were five studies by the group of Edgerton et al. who report on overlapping patients [21–25]. Therefore their papers of 2007 and 2008 have been excluded from analysis in calculations of complications [21,22]. The paper of Wang et al. [31] describes an open-label randomized trail where patients received irbesartan after minimally-invasive surgery. For calculations of the cumulative results only the patients not receiving irbesartan were selected. There were two studies by the group of Speziale and Nasso, who performed a monolateral thoracotomy. As this procedure has different surgical approach, it has been excluded from the cumulative analysis, but the results of these studies can be found in Tables 2 and 3.

Table 1
Search query.

Database	Search query	Search results
Pubmed	(atrial fibrillation[tiab] OR AF[tiab]) AND (epicardial ablation[tiab] OR endoscopic[tiab] OR thoracoscopic [tiab] OR videothoracoscopy[tiab] OR surgical ablation [tiab] OR minimally invasive[tiab] OR minimal invasive [tiab] OR mini-maze[tiab] OR VATS[tiab] OR epicardial pulmonary vein isolation[tiab] OR surgical pulmonary vein isolation[tiab])	Total: 538 Exclusion: 32 Inclusion: 21
Embase	("atrial fibrillation":ti,ab OR "AF":ti,ab) AND ("epicardial ablation":ti,ab OR "endoscopic":ti,ab OR "thoracoscopic": ti,ab OR "videothoracoscopy":ti,ab OR "surgical ablation": ti,ab OR "minimal invasive":ti,ab OR "minimally invasive": ti,ab OR "mini-maze":ti,ab OR "VATS":ti,ab OR "epicardial pulmonary vein isolation":ti,ab OR "surgical pulmonary vein isolation":ti,ab)	Total: 632 Exclusion: 43 Inclusion: 23

The search was performed on 07-07-2011.
Exclusion criteria: Animal studies, reviews, case reports, concomitant surgery, not atrial fibrillation, not minimally-invasive surgery, not English, no full-text availability.
Inclusion criteria: Studies with >10 patients, follow-up of >3 months, use of radio frequent energy, off-pump cardiac surgery.

3.1. Surgery

In all but two studies bilateral thoracotomy or thorascopic approach to surgery was performed, only the group of Speziale and Nasso used a monolateral thoracotomy [12,16]. Two studies performed a hybrid procedure; Krul et al. [30] performed extensive electrophysiological measurements epicardially while Pison et al. performed simultaneous transvenous catheter measurements. There were differences in the execution of the minimally-invasive surgical procedure (Table 2). RF energy was used in all studies as this was a selection criterion in including the studies in this paper. GP ablation was performed in 14 of 22 studies in addition to PVI (Table 2). Irrespective of the choice of GP ablation the ligament of Marshall was divided in all but two studies [12,16]. ALAL were made in four studies as shown in Table 2 [17,23,30]. The LAA was excluded through suturing or stapling in 20 of 22 studies [5,13–15,17–31,34]. From studies of which procedure data were available, the mean procedure duration is 208 minutes (n = 12 studies [5,13,14,17–20,26,28,30,31]) and hospital admission is 5 days (n = 17 studies [5,13,14,17–20,23–28,30,31,34]).

3.2. Outcome

Definition of success varied between studies, but unfortunately not all studies report according to the HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of AF (Tables 2 and 3) [35].

All papers present a total number of patients of 842 who underwent surgery. The reported population comprised of 752 patients. This number is lower because some patients were lost for follow-up or were still in the 3 months blanking period following the procedure at the time of publication.

In these studies a mean of 26% (range 5%–45%, n = 15 studies) of patients had a history of a previous catheter ablation (excluding Castella et al. [27], where all patients had a previous catheter ablation). Total follow up varied from 2 to 45 months, with a reported mean ranging from 5.7–18 months. Unfortunately 6 month and/or 12 month follow-up were not reported in all studies. It was not always possible to assess the success percentage at these times of follow up. Results in the different types of AF and the use of AAD were not specified in every study and as such not all studies could be included in the respective pooled analysis.

Given these restrictions, the overall single procedure success rate of minimally-invasive surgery without AAD is 64% (95% CI, range 55%–72%, n = 7 studies) at a follow-up of 6 months and 69% (95% CI, range 58%–78%, n = 5 studies) at 12 months follow-up.

With AAD the single procedure success rate was 75% (95% CI, range 70%–80%, n = 5 studies) the 6-months of follow up (Fig. 1). At 12-months success rate was comparable at 79% (95% CI, range 71%–85%, n = 7 studies) with AAD (Fig. 1).

In studies with GP ablation the overall success rate is 63% with AAD (95% CI, range 58%–69%, n = 15 studies) while in studies where the investigators refrained from GP ablation, the success rate was 83% with AAD (95% CI, range 63%–94%, n = 6 studies).

In studies with ALAL the overall success rate is 77% with AAD (95% CI, range 53%–92%, n = 4 studies) while in studies where the

Table 2
Minimally-invasive surgery for atrial fibrillation: studies overview.

First author	Year	No of centres	GP ablation	ALAL ablation	AF endpoints	Follow up	Rhythm monitoring
Wolf [5]	2005	Single	No	No	Not specified	Office visits, medical records, telephone calls to the patients, records from cardiology visits	ECG, outpatient telemonitoring
Sagbas [18]	2006	Single	No	No	Not specified	End of the surgical procedure, 3 months and 6 months	ECG, Holter
Edgerton [21]	2007	Single	Yes	No	No episodes of AF longer than 15 seconds at 6 months	Outpatient visit at 1, 3 and 6 months	ECG, Holter, event recorder, pacemaker
Wudel [14]	2007	Single	No	No	Not specified	Outpatient visit at 3, 6, 12 months, and then until end of study	ECG, Holter
McClelland [34]	2007	Single	Yes	No	Free of AAD (class IC and III) and AF, no more than 30 seconds of AF after 3 months	Outpatient visit at 1, 2, 3, 6 weeks, and 3, 6 months, then every 6 months	ECG, Holter, event recorder
Matsutani [19]	2008	Two	Yes	No	Not specified	Not specified	ECG, questionnaires
Edgerton [22]	2008	Single	Yes	No	No episodes of AF longer than 15 seconds at 6 months	Outpatient visit at 1, 3 and 6 months	ECG, Holter, event recorder, pacemaker
Sirak [17]	2008	Single	Yes	Yes[a]	No episode of AF or AFT lasting 30 s after blanking period of 3 months	Outpatient visit 3, 6 and 13 months	ECG, event recorder
Beyer [28]	2009	Three	Yes	No	Absence of AF or AFT on ECG and Holter	Not specified	ECG, Holter
Edgerton [24]	2009	Multi	Yes	No	No episodes of AF and no AAD	Outpatient visit at 1, 3 and 6 months	ECG, Holter, event recorder, pacemaker
Bagge [29]	2009	Single	Yes	No	No documented symptomatic AF or AT after 12 months of follow up on ECG, 24 h Holter and spot ECG	Outpatient visit at 3, 6 and 12 months	ECG, Holter
Han [20]	2009	Single	Yes	No	No AF /AFT/AT more than 30 s on ECG or Holter monitoring off AAD	Outpatient visit at 6, 12 months and 12 months thereafter	ECG, Holter, event recorder, pacemaker
Edgerton ELS [23]	2009	Single	Yes	Yes[b]	No episodes of AF/AFT/AT more than 15 s during monitoring at 6 months	Outpatient visit at 1, 3, and 6 months	ECG, event recorder
Edgerton [25]	2010	Two	Yes	No	No episodes of AF/AFT/AT more than 30 s on ECG or Holter monitoring	Outpatient visit at 1, 3, 6 and 12 months	ECG, Holter, event recorder, pacemaker
Speziale [16]	2010	Single	No	No	Absence of AF or other SVT 6 months after surgery on Holter	Outpatient visit at 3, 6 and 12 months	ECG, Holter, echocardiogram
Cui [26]	2010	Single	No	No	No AF or AFT more than 30 s on ECG or Holter monitoring	Outpatient visit at 1, 3, 6 and 12 months	ECG, Holter, echo, pacemaker
Castella [27]	2010	Single	No	No	No symptomatic episode of arrhythmia or SVT lasting more than 30 s in any ECG or Holter	Outpatient visit at 1, 4, 6 and 12 months	ECG, Holter, echo
Stamou [15]	2010	Single	Yes	No	Not specified	Not specified	Not specified
Yilmaz [13]	2010	Single	Yes	No	No episode of AF more than 30 s after blanking period of 3 months	Outpatient visit at 1 and 3 weeks and 3, 6, 12 months	ECG, Holter, refering physician
Krul [30]	2011	Single	Yes	Yes[c]	No AF/AFT/AT more than 30 s on ECG or Holter monitoring of AAD	Outpatient visit at 3, 6, 12, 15, 18, 24 months	ECG, Holter, MRI
Pison	2011	Single	Yes	Yes[d]	No AF/AFT/AT more than 30 s on ECG or Holter monitoring of AAD	Outpatient visit at 3, 6 and 12 months	ECG, Holter
Wang [31]	2011	Single	Yes	No	No AF/AFT more than 30 s on ECG or Holter monitoring	Outpatient visit at 1, 3, 6, and 12 months for clinical interview,	ECG, Holter, echocardiogram
Nasso [12]	2011	Single	No	No	One year clincical results of rate of recurrence of AF, freedom from, antiarrhytmic medications	Outpatient visit at 3, 6 and 12 months	ECG, Holter, echocardiogram

AAD: antiarrhythmic drugs, AF: atrial fibrillation, AFT: atrial flutter, ALAL: additional left atrial lesions, AT: atrial tachycardia, GP: ganglionic plexus, ELS: extended lesion set, LAA: left atrial appendage, SVT: supraventricular tachycardia.

[a] Left atrial appendage line and mitral line.

[b] Roof line, trigone line and left atrial appendage line.

[c] Roof line, inferior line and trigone line.

[d] Roof line, inferior line and optional left isthmus line and right atrial lines.

Table 3
Minimally-invasive surgery for atrial fibrillation: patient number and results overview of studies.

First author	Year	Operated patients[a]	FU (months)	Overall			Paroxysmal AF			Persistent AF			LSP AF		
				Total	%		Total	%		Total	%		Total	%	
					AAD	No AAD		AAD	No AAD		AAD	No AAD		AAD	No AAD
Wolf [5]	2005	29	5.7	23	**91**	**65**	–	–	–	–	–	–	–	–	–
Sagbas [18]	2006	26	6	26	–	**81**	–	**100**	**100**	–	**72**	**72**	–	–	–
Edgerton [21]	2007	83	6	57	**74**	**63**	39	**82**	**74**	18	**56**	**39**	–	–	–
Wudel [14]	2007	23	18	22	–	**91**	–	–	**–**	**–**	**–**	**–**	**–**	**–**	**–**
McClelland [34]	2007	20	12	20	**–**	**75**	**–**	**91**	**91**	–	**80**	**80**	4	**25**	**25**
Matsutani [19]	2008	20	16,6	20	**90**	**85**	–	–	–	–	–	–	–	–	–
Edgerton [22]	2008	74	6	66	**74**	**58**	43	**84**	**70**	23	**57**	**35**	–	**–**	**–**
Sirak [17]	2008	32	6	24	**–**	**88**	–	–	–	–	–	–	–	–	–
Beyer [28]	2009	100	13.6	100	**87**	**63**	39	**93**	–	29	**96**	–	–	**71**	–
Edgerton [24]	2009	114	6	114	**71**	**57**	60	**87**	**72**	32	**56**	**47**	22	**50**	**32**
Bagge [29]	2009	43	12	33	**76**	**52**	24	**79**	–	2	**100**	–	–	**57**	–
Han [20]	2009	45	12	43	–	**65**	–	**70**	**70**	–	**58**	**58**	–	–	–
Edgerton ELS [23]	2009	30	6	30	**80**	**47**	–	–	–	10	**90**	**70**	20	**75**	**35**
Edgerton [25]	2010	52	12	52	**81**	**63**	52	**81**	**63**	–	–	–	–	–	–
Speziale [16]	2010	54	6	46	**87**	–	19	**95**	–	27	**81**	–	–	–	–
Cui [26]	2010	81	12	49	**80**	–	–	**80**	–	–	**75**	–	–	**67**	–
Castella [27]	2010	38	12	26	**62**	–	11	**82**	–	10	**60**	–	–	**20**	–
Stamou [15]	2010	20	12	12	**75**	–	7	**100**	–	5	**40**	–	–	–	–
Yilmaz [13]	2010	30	11.6	30	**77**	**50**	19	**84**	–	8	**75**	–	–	**33**	–
Krul [30]	2011	31	12	22	**91**	**86**	12	**100**	**92**	9	**78**	**78**	1	**100**	**100**
Pison	2011	26	12	24	**92**	**83**	14	**93**	**79**	11	**90**	**90**	–	–	–
Wang [31]	2011	83	24	81	–	**80**	–	–	–	–	–	–	81	–	**80**
Nasso [12]	2011	104	12	104	**89**	**53**	–	**96**	–	–	**80**	–	–	–	–

AAD: antiarrhythmic drugs, AF: atrial fibrillation, ELS: extended lesion set, FU: follow-up, LSP AF: long standing persistent atrial fibrillation.
[a] Total number of patients who underwent the procedure is higher than overall reported patients because some patients did not complete the procedure or were still in the 3 months blanking period during publication.

investigators performed only PVI, the success rate was 65% with AAD (95% CI, range 60%–70%, n = 16 studies).

Specified to the different type of AF, success in paroxysmal AF was 71% (95% CI, range 65%–77%, n = 5 studies), persistent AF 51% (95% CI, range 36%–65%, n = 5 studies) (Fig. 2) and for LSP AF 33% (95% CI, range 21%–49%, n = 2 studies) at 6 months (Fig. 2). Success at 12 months with paroxysmal AF was 75% (95% CI, range 66%–82%, n = 8 studies) and 67% (95% CI, range 52%–79%, n = 7 studies) in persistent AF (Fig. 2) and 43% (95% CI, range 21%–68%, n = 4 studies) in LSP AF.

3.3. Complications

Three casualties have been reported during or within 30 days after the procedure. One occurred during the procedure as a consequence of tearing of the LAA. For one death, the day after the procedure, the cause of death was undetermined and lastly, one late death resulted from cerebral infarction 30 days after the procedure. While mortality is low, surgical and post-procedural complications are relatively more frequently encountered. In 1.7% (14/842) of the procedures a sternotomy was required to control bleeding. Predominantly surgical complications of 3.2%, post-surgical complications of 3.2% and cardiac complications of 2.6% were described in the selected papers. A full list of morbidity related to the minimally-invasive procedure is listed in Table 4.

4. Discussion

4.1. Minimally-invasive surgery

This systematic review comprises the first cumulative results of minimally-invasive surgery. These studies report an overall single procedure success rate of 69% without AAD and 79% with AAD at one year. Interestingly the results at 6 months are somewhat lower (64% without AAD and 75% with AAD) (Fig. 3). There can be two explanations for this finding; firstly studies reporting results at 6 months follow-up represent the very first published reports of minimally-invasive surgery as can be appreciated from Table 3. Secondly not all people are weaned of their AAD at 6 months after the procedure. Most studies in this review use similar methods and have a mixed AF population (paroxysmal, persistent and LSP). Only one paper describes the results in a group of paroxysmal AF [25] and three papers in only persistent and LSP AF [17,23,31]. Minimally-invasive surgery is most effective in paroxysmal AF, but even in persistent AF and LSP AF more than half of the patients benefit from minimally-invasive surgery (Fig. 2). A recurrence of AF over time appears to be present, similar to the time course of recurrences after catheter ablation [36]. Invasive ablation of AF is helpful to the majority of selected patients, but the disease progresses and causes recurrences in part of the patients. Comparison between catheter based PVI and minimally-invasive surgery is not possible; first, these are the first cumulative results of minimally-invasive surgery and secondly, no randomized control trial has been published comparing these two treatment modalities. Yet, while minimally-invasive PVI appear at least equally successful, catheter based PVI and minimally-invasive surgery have the same limitation. Both treatment strategies only aim to eliminate a trigger of AF, namely ectopic triggers from the pulmonary veins. Recently substrate modification with the use of additional left atrial lines has been proposed to increase success rates in non-paroxysmal AF.

A substantial part of the population reported in the papers had one or more previous catheter ablation (mean 26%). This might influence the results with minimally-invasive surgery; these patients might have incomplete lesions leading to AT, which are difficult to treat because these lesions are not easily identifiable. However the pre-existent substrate modification and PVI ablation might also increase the success rate of minimally-invasive surgery. Interestingly, Castella et al. [27] have, compared to other investigators, a moderate procedural success rate (62% with AAD), but they report results of patients with an earlier failed catheter-PVI only. These patients might have had different substrates in which PVI does not eliminate the pathophysiologic mechanism completely.

Speziale et al. and Nasso et al. [12,16] used a monolateral approach and only performed PVI, without electrophysiological measurements.

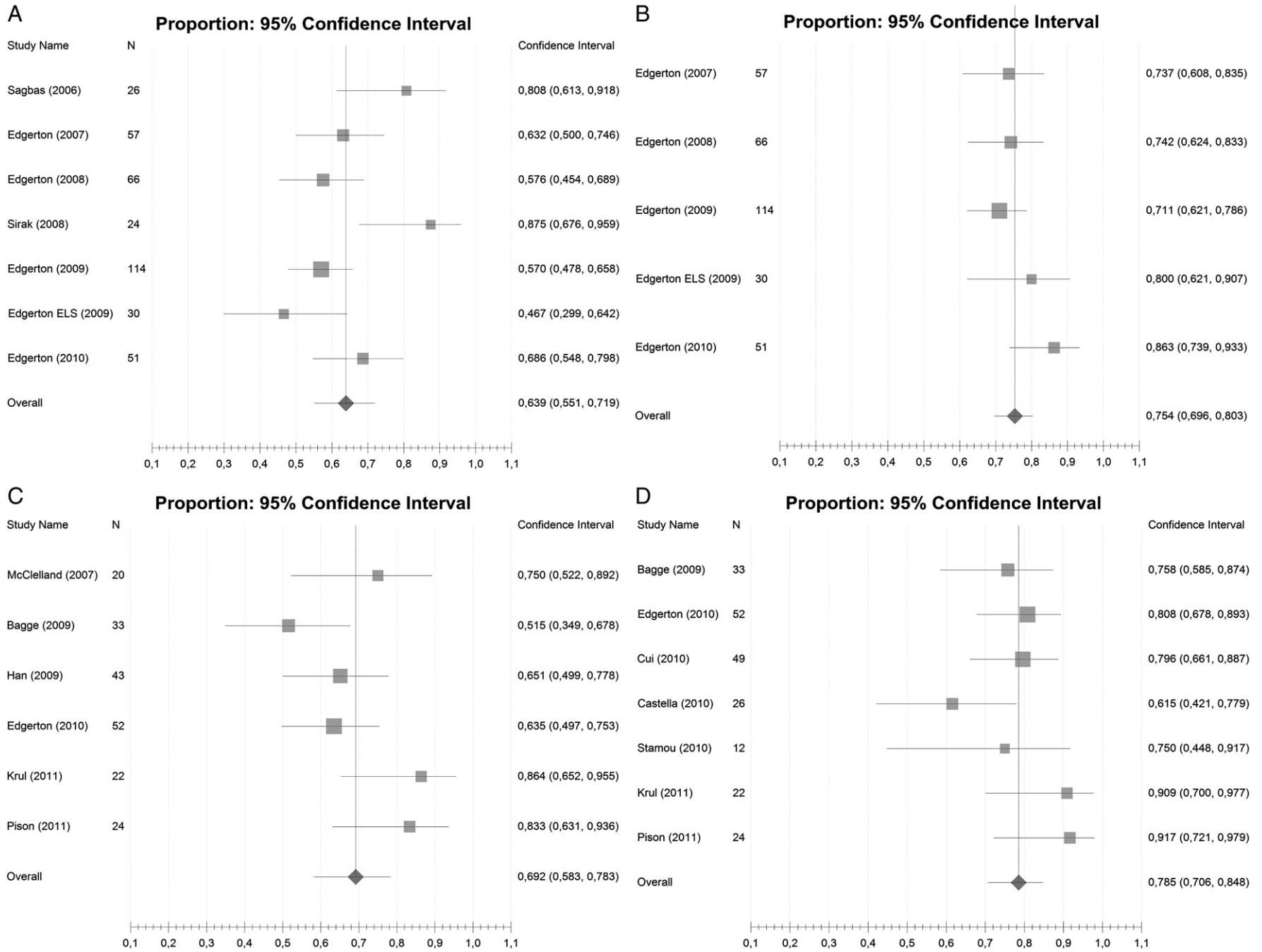


Fig. 1. This figure shows four forest plots representing the proportion of the patients in sinus rhythm at 6 months and 12 months. The top left plot shows the results at 6 months without AAD (n = 7 studies) and the top right at 6 months with AAD (n = 6 studies). The bottom left plot shows the results at 12 months without AAD (n = 6 studies) and the bottom right with AAD (n = 7 studies). Note that the 6 months results are mostly results from studies of Edgerton et al. AAD: antiarrhythmic drugs.

With this technique they achieve an average success rate with a low risk of procedure related-morbidity. Currently there is no confirmatory experience with this technique. Two studies perform periprocedural electrophysiological confirmation of conduction block of PVI and ALAL. Krul et al. [30] use epicardial confirmation of conduction block while Pison et al. use a endovascular approach. These studies demonstrate that electrophysiological measurements are feasible during minimally-invasive surgery and that this hybrid approach might increase the success rate of minimally-invasive surgery [37].

4.2. Role of GP ablation

There is ample evidence from animal studies that neurohumoral influence on the PVs plays an important role in the initiation of AF [6]. Although the precise role of GPs has not yet been established, the minimally-invasive approach offers access to the epicardial fat pads where the GPs reside and allows their ablation. Additional GP ablation can be performed to modify the local neurohumoral triggers of the atria and it has been hypothesized that this might decrease recurrence of AF. During epicardial surgery localization both visually and with high frequency stimulation and subsequent ablation of the GPs is possible. The absence of a vagal response to high frequency stimulation after ablation is generally considered proof of destruction of the GP. GP ablation has been added as a routine part of the minimally-invasive surgery protocol for AF by some investigators. However its value in the epicardial treatment of AF has not been established. There is evidence that endocardial ablation of GPs might increase success rate of catheter PVI. A vagal response during a catheter PVI procedure is associated with a lower recurrence of AF [38]. In the studies reviewed here, there is a difference between GP ablation (63%) and no GP ablation (83%) in the addition to PVI. This might indicate that GP ablation is not an essential part in the minimally-invasive surgery of AF to prevent recurrence of AF. Clearly, follow-up was short and at the present these data do not allow to draw any meaningful clinical conclusions, and this difference merely underscores the need for further randomized studies.

4.3. Role of left atrial lesions

Four studies have been published that report the creation of an additional lesion set on the left atrium [17,23,30]. The types of lesions are not uniform in these studies but compartmentalization of the posterior left atrium, to prevent re-entry around the PVs, is the hallmark of these lesions. These lesions purposefully increase the success rate in patients with persistent and LSP AF. From results with catheter ablation therapy it is suggested that only PVI in these patient may not be sufficient to prevent recurrence of AF [39]. The application of RF energy and subsequent visualization of the lines is possible in minimally-invasive surgery. In our view, additional electrophysiological testing is required to assess complete block over these lines [40]. It has been demonstrated in two studies that a large proportion of patients undergoing minimally-invasive surgery might suffer from atrial tachycardias [41,42]. Therefore all effort should be taken to produce a lesion set that actually demonstrates conduction block. Although longer follow-up is needed, a comprehensive set of left atrial lesions might increase freedom of AF in patients with persistent or LSP AF. A reproducible set of lesions with peri-operative proof of block can therefore be a valuable addition to the minimally-invasive procedure. Thus the types of left atrial lesions that are most effective, are easy reproducible, and can be thoroughly tested electrophysiologically, should be investigated and their value in the different types of AF should be assessed.

4.4. Mortality and morbidity

Due to the epicardial approach to PVI minimally-invasive surgery incurs other risk in comparison with catheter PVI. There is for example a risk of conversion to on-pump cardiac surgery due to thoracoscopic surgery on the beating heart. However there is no radiation exposure during the procedure and therefore there are no radiation related complications. Mortality is limited, especially compared to other cardiac operations, and appears to be similar with catheter PVI (incidence minimally-invasive 0.4% vs. catheter ablation 0.7%) [39]. Surgical and post-procedural complications are frequently encountered (Table 4). As can be appreciated from this table the risks of minimally-invasive surgery are mainly peri-procedural problems followed by cardiac and pulmonary complications. These complication rates can be explained through the procedural difficulty and the learning curve of the surgery. Even though most complications are transient, the risk of pacemaker implantation of 1.4% is substantial. Furthermore there is still a risk of stroke or TIA (0.5%) during or shortly after minimally-invasive surgery. This risk of occurrence is not abolished through epicardial ablation, but it is smaller than in catheter based PVI [39]. The anti-coagulation policy before and after surgery (when the LAA is excluded) is difficult; the balance between prevention of embolic events versus prevention of bleeding complications is precarious. There is little evidence of how to manage anti-coagulation after the treatment of AF and guidelines currently suggest maintaining anti-coagulation based on the CHA_2DS_2VASc score [39].

4.5. Future developments

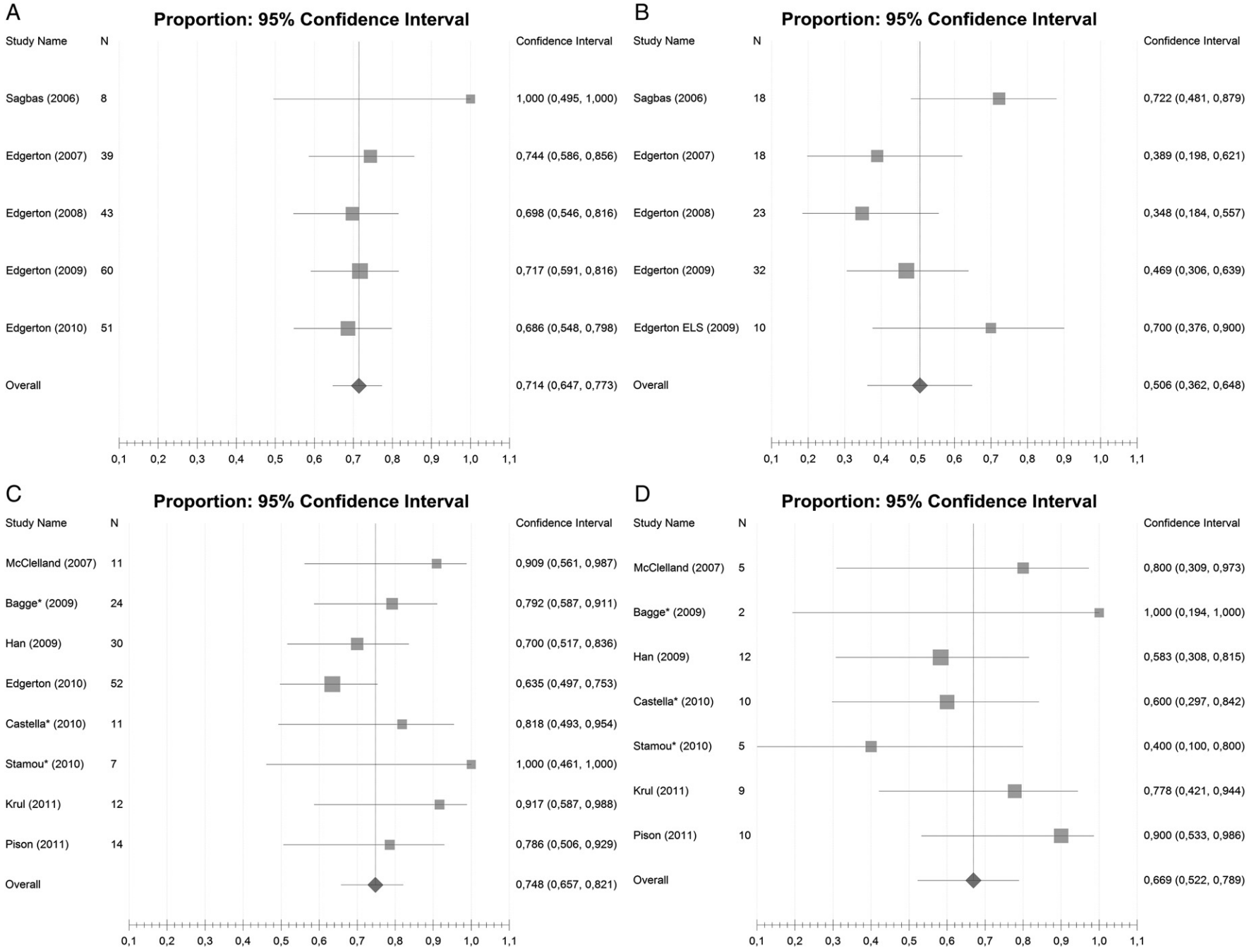
The position of minimally-invasive surgery in the treatment of AF treatment has yet to be established. The results presented in this paper show the first results of minimally-invasive surgery. As such the potential of minimally-invasive surgery is still to be realized. Outcomes may benefit from standardization of the technique, results of longer follow-up and an improved patients selection. Furthermore recent incorporation of electrophysiological measurements by some groups might increase the success rates the procedure. At the moment there are two ongoing studies comparing minimally-invasive surgery with catheter based PVI (SCALAF-trail and the FAST-trail). In these studies the two treatment modalities are compared with each other, but a complementary role of these interventions might be envisioned. Patient preference can be the decisive factor in choosing catheter ablation or minimally-invasive surgery when comparing both the risks and the benefits of the two different approaches.

4.6. Limitations

This systematic review did not have access to all individual patient data and therefore our results and conclusions are based on published data. Furthermore not all results are reported according to the HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation [35] which makes a comparison of the different studies difficult. Due to the increasing experience and knowledge with minimally-invasive surgery, the technique has evolved significantly after the first publication. Results of the first studies might not be fully comparable to those published later. Furthermore, this paper is an overview of minimally-invasive surgery based on published reports and therefore might be subject to publication bias and might not reflect current practice in individual centres.

5. Conclusions

Minimally-invasive surgery is a new invasive procedure for the non-pharmaceutical treatment of AF. The first studies describe a


A
Proportion: 95% Confidence Interval
Study Name N Confidence Interval
Sagbas (2006) 8 1,000 (0,495, 1,000)
Edgerton (2007) 39 0,744 (0,586, 0,856)
Edgerton (2008) 43 0,698 (0,546, 0,816)
Edgerton (2009) 60 0,717 (0,591, 0,816)
Edgerton (2010) 51 0,686 (0,548, 0,798)
Overall 0,714 (0,647, 0,773)
0,1 0,2 0,3 0,4 0,5 0,6 0,7 0,8 0,9 1,0 1,1
B
Proportion: 95% Confidence Interval
Study Name N Confidence Interval
Sagbas (2006) 18 0,722 (0,481, 0,879)
Edgerton (2007) 18 0,389 (0,198, 0,621)
Edgerton (2008) 23 0,348 (0,184, 0,557)
Edgerton (2009) 32 0,469 (0,306, 0,639)
Edgerton ELS (2009) 10 0,700 (0,376, 0,900)
Overall 0,506 (0,362, 0,648)
0,1 0,2 0,3 0,4 0,5 0,6 0,7 0,8 0,9 1,0 1,1
C
Proportion: 95% Confidence Interval
Study Name N Confidence Interval
McClelland (2007) 11 0,909 (0,561, 0,987)
Bagge* (2009) 24 0,792 (0,587, 0,911)
Han (2009) 30 0,700 (0,517, 0,836)
Edgerton (2010) 52 0,635 (0,497, 0,753)
Castella* (2010) 11 0,818 (0,493, 0,954)
Stamou* (2010) 7 1,000 (0,461, 1,000)
Krul (2011) 12 0,917 (0,587, 0,988)
Pison (2011) 14 0,786 (0,506, 0,929)
Overall 0,748 (0,657, 0,821)
0,1 0,2 0,3 0,4 0,5 0,6 0,7 0,8 0,9 1,0 1,1
D
Proportion: 95% Confidence Interval
Study Name N Confidence Interval
McClelland (2007) 5 0,800 (0,309, 0,973)
Bagge* (2009) 2 1,000 (0,194, 1,000)
Han (2009) 12 0,583 (0,308, 0,815)
Castella* (2010) 10 0,600 (0,297, 0,842)
Stamou* (2010) 5 0,400 (0,100, 0,800)
Krul (2011) 9 0,778 (0,421, 0,944)
Pison (2011) 10 0,900 (0,533, 0,986)
Overall 0,669 (0,522, 0,789)
0,1 0,2 0,3 0,4 0,5 0,6 0,7 0,8 0,9 1,0 1,1

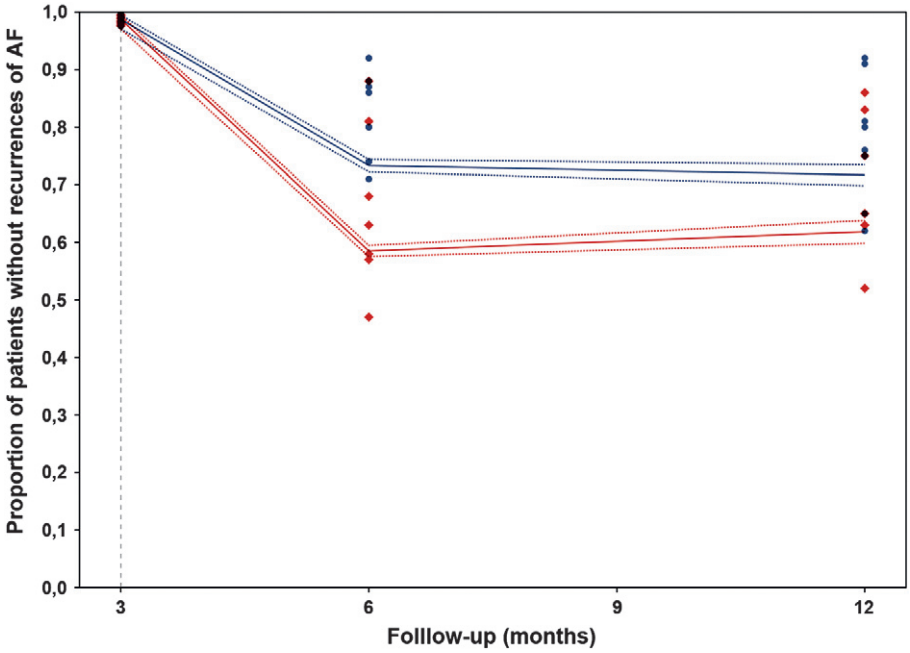


Fig. 3. Overall freedom from atrial fibrillation curve for minimally-invasive surgery. This figure shows the overall freedom of AF curve for minimally-invasive surgery using the reported proportions in the published papers at 6 months and 12 months. The blue line represents the overall results with AAD. The blue dotted line is the confidence interval of the overall results. Blue circles (●) represent the different studies and their outcome. Red lines and diamonds (♦) represent results without AAD. AAD: antiarrhythmic drugs, AF: atrial fibrillation.

Table 4
Minimally-invasive surgery for atrial fibrillation: morbidity.

Morbidity	N = 842	
Surgical complications	27	3.20%
Conversions	14	1.70%
Conversions requiring heart-lung machine	4	0.50%
Bleeding	12	1.40%
LA Bleeding	5	0.60%
PV bleeding	4	0.50%
LAA bleeding	3	0.40%
Other complications	1	0.10%
Post-surgical complications	27	3.20%
Hematothorax	12	1.40%
Nerve injury	10	1.20%
Wound problems	4	0.50%
Ribfracture	1	0.10%
Cardiac complications	22	2.60%
Pacemaker implantation	12	1.40%
Pericarditis	5	0.60%
Ventricular arrhythmias	3	0.40%
Cardiac effusion	2	0.20%
Pulmonary complications	18	2.10%
Ventilation support	9	1.10%
Pneumothorax	5	0.60%
Pulmonary embolism	2	0.20%
Pleural effusion	2	0.20%
Other complications	14	1.70%
Infection	6	0.70%
Stroke/TIA	4	0.50%
Renal insufficiency	4	0.50%
Minor complications	3	0.40%
Phlebitis	1	0.10%
Coagluation problems	1	0.10%
Delirium	1	0.10%

LA: left atrium, LAA: left atrial appendage, PV: pulmonary vein, TIA: transient ischemic attack.

single procedure success rate of 69% without AAD and 79% with AAD at one year follow-up. These results show a promising role for minimally-invasive surgery, although these results are likely to increase as the procedure progresses. Similar to catheter ablation it has a higher success rate in paroxysmal AF. Electrophysiological measurements and confirmation of the ablation lines might be an important factor to increase the success of this procedure. Additional research in the creation and type of left atrium lines in patients with persistent and LSP AF should determine a reproducible and effective left atrial lesion set to prevent recurrences in these types AF. Furthermore, the additional value of GP ablation is to be elucidated to asses its role in minimally-invasive surgery.

Funding

Netherlands Heart Foundation, 2009T021.

Conflicts of interest

J.R. de Groot, supported by a personal grant from the Netherlands Heart Foundation, 2009T021.

Acknowledgement

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

Fig. 2. This figure shows four forest plots representing the proportion of the patients in sinus rhythm at 6 months and 12 months specified to the different types of AF. The forest plot at the top show the results at 6 months of paroxysmal AF (n = 6 studies) and persistent AF (n = 6 studies).The bottom plots show the results at 12 months of paroxysmal AF (n = 9 studies) and persistent AF (n = 8 studies) Of the studies marked with an asterisk (*) only results with the use of antiarrhythmic drugs are available. AF; atrial fibrillation.

References

[1] Cox JL, Jaquiss RD, Schuessler RB, et al. Modification of the maze procedure for atrial flutter and atrial fibrillation. II. Surgical technique of the maze III procedure. J Thorac Cardiovasc Surg 1995;110:485–95.

[2] Cox JL, Boineau JP, Schuessler RB, et al. Modification of the maze procedure for atrial flutter and atrial fibrillation. I. Rationale and surgical results. J Thorac Cardiovasc Surg 1995;110:473–84.

[3] Haissaguerre M, Jais P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998;339: 659–66.

[4] Calkins H, Reynolds MR, Spector P, et al. Treatment of atrial fibrillation with antiarrhythmic drugs or radiofrequency ablation: two systematic literature reviews and meta-analyses. Circ Arrhythm Electrophysiol 2009;2:349–61.

[5] Wolf RK, Schneeberger EW, Osterday R, et al. Video-assisted bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. J Thorac Cardiovasc Surg 2005;130:797–802.

[6] Scherlag BJ, Yamanashi W, Patel U, et al. Autonomically induced conversion of pulmonary vein focal firing into atrial fibrillation. J Am Coll Cardiol 2005;45: 1878–86.

[7] Pruitt JC, Lazzara RR, Ebra G. Minimally invasive surgical ablation of atrial fibrillation: the thoracoscopic box lesion approach. J Interv Card Electrophysiol 2007;20: 83–7.

[8] Pruitt JC, Lazzara RR, Dworkin GH, et al. Totally endoscopic ablation of lone atrial fibrillation: initial clinical experience. Ann Thorac Surg 2006;81:1325–30.

[9] Koistinen J, Valtonen M, Savola J, et al. Thoracoscopic microwave ablation of atrial fibrillation. Interact Cardiovasc Thorac Surg 2007;6:695–8.

[10] Klinkenberg TJ, Ahmed S, Ten HA, et al. Feasibility and outcome of epicardial pulmonary vein isolation for lone atrial fibrillation using minimal invasive surgery and high intensity focused ultrasound. Europace 2009;11:1624–31.

[11] Wallace BC, Schmid CH, Lau J, et al. Meta-Analyst: software for meta-analysis of binary, continuous and diagnostic data. BMC Med Res Methodol 2009;9:80.

[12] Nasso G, Bonifazi R, Del PA, et al. Long-term results of ablation for isolated atrial fibrillation through a right minithoracotomy: Toward a rational revision of treatment protocols. J Thorac Cardiovasc Surg 2011;142:e41–6.

[13] Yilmaz A, Geuzebroek GS, Van Putte BP, et al. Completely thoracoscopic pulmonary vein isolation with ganglionic plexus ablation and left atrial appendage amputation for treatment of atrial fibrillation. Eur J Cardiothorac Surg 2010;38:356–60.

[14] Wudel JH, Chaudhuri P, Hiller JJ. Video-assisted epicardial ablation and left atrial appendage exclusion for atrial fibrillation: extended follow-up. Ann Thorac Surg 2008;85:34–8.

[15] Stamou SC, Khabbaz KR, Mahmood F, et al. A multidisciplinary approach to the minimally invasive pulmonary vein isolation for treatment of atrial fibrillation. Ann Thorac Surg 2010;89:648–50.

[16] Speziale G, Bonifazi R, Nasso G, et al. Minimally invasive radiofrequency ablation of lone atrial fibrillation by monolateral right minithoracotomy: operative and early follow-up results. Ann Thorac Surg 2010;90:161–7.

[17] Sirak J, Jones D, Sun B, et al. Toward a definitive, totally thoracoscopic procedure for atrial fibrillation. Ann Thorac Surg 2008;86:1960–4.

[18] Sagbas E, Akpinar B, Sanisoglu I, et al. Video-assisted bilateral epicardial pulmonary vein isolation for the treatment of lone atrial fibrillation. Ann Thorac Surg 2007;83: 1724–30.

[19] Matsutan N, Takase B, Ozeki Y, et al. Therapeutic strategy for atrial fibrillation by minimally invasive surgery using athoracoscopic mini maze procedure. Ther Res 2009;30:1129–32.

[20] Han FT, Kasirajan V, Kowalski M, et al. Results of a minimally invasive surgical pulmonary vein isolation and ganglionic plexi ablation for atrial fibrillation: single-center experience with 12-month follow-up. Circ Arrhythm Electrophysiol 2009;2:370–7.

[21] Edgerton JR, Jackman WM, Mack MJ. Minimally invasive pulmonary vein isolation and partial autonomic denervation for surgical treatment of atrial fibrillation. J Interv Card Electrophysiol 2007;20:89–93.

[22] Edgerton JR, Edgerton ZJ, Weaver T, et al. Minimally invasive pulmonary vein isolation and partial autonomic denervation for surgical treatment of atrial fibrillation. Ann Thorac Surg 2008;86:35–8.

[23] Edgerton JR, Jackman WM, Mahoney C, et al. Totally thorascopic surgical ablation of persistent AF and long-standing persistent atrial fibrillation using the "Dallas" lesion set. Hear Rhythm 2009;6:S64–70.

[24] Edgerton JR, McClelland JH, Duke D, et al. Minimally invasive surgical ablation of atrial fibrillation: six-month results. J Thorac Cardiovasc Surg 2009;138: 109–13.

[25] Edgerton JR, Brinkman WT, Weaver T, et al. Pulmonary vein isolation and autonomic denervation for the management of paroxysmal atrial fibrillation by a minimally invasive surgical approach. J Thorac Cardiovasc Surg 2010;140:823–8.

[26] Cui YQ, Li Y, Gao F, et al. Video-assisted minimally invasive surgery for lone atrial fibrillation: a clinical report of 81 cases. J Thorac Cardiovasc Surg 2010;139: 326–32.

[27] Castella M, Pereda D, Mestres CA, et al. Thoracoscopic pulmonary vein isolation in patients with atrial fibrillation and failed percutaneous ablation. J Thorac Cardiovasc Surg 2010;140:633–8.

[28] Beyer E, Lee R, Lam BK. Point: minimally invasive bipolar radiofrequency ablation of lone atrial fibrillation: early multicenter results. J Thorac Cardiovasc Surg 2009;137:521–6.

[29] Bagge L, Blomstrom P, Nilsson L, et al. Epicardial off-pump pulmonary vein isolation and vagal denervation improve long-term outcome and quality of life in patients with atrial fibrillation. J Thorac Cardiovasc Surg 2009;137:1265–71.

[30] Krul SP, Driessen AH, Van Boven WJ, et al. Thoracoscopic Video-Assisted Pulmonary Vein Antrum Isolation, Ganglionated Plexus Ablation and Periprocedural Confirmation of Ablation Lesions. First Results of a Hybrid Surgical-Electrophysiological Approach for Atrial Fibrillation. Circ Arrhythm Electrophysiol 2011;4:262–70.

[31] Wang JG, Li Y, Shi JH, et al. Treatment of long-lasting persistent atrial fibrillation using minimally invasive surgery combined with irbesartan. Ann Thorac Surg 2011;91:1183–9.

[32] Colafranceschi AS, Monteiro AJ, Botelho ES, et al. Videothoracoscopy for isolated atrial fibrillation ablation through bipolar radiofrequency. Arq Bras Cardiol 2009;93:334–5.

[33] Li H, Li Y, Sun L, et al. Minimally invasive surgical pulmonary vein isolation alone for persistent atrial fibrillation: preliminary results of epicardial atrial electrogram analysis. Ann Thorac Surg 2008;86:1219–25.

[34] McClelland JH, Duke D, Reddy R. Preliminary results of a limited thoracotomy: new approach to treat atrial fibrillation. J Cardiovasc Electrophysiol 2007;18:1289–95.

[35] Calkins H, Brugada J, Packer DL, et al. HRS/EHRA/ECAS expert Consensus Statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. A report of the Heart Rhythm Society (HRS) Task Force on catheter and surgical ablation of atrial fibrillation. Hear Rhythm 2007;4:816–61.

[36] Weerasooriya R, Khairy P, Litalien J, et al. Catheter ablation for atrial fibrillation are results maintained at 5 years of follow-up? J Am Coll Cardiol 2011;57:160–6.

[37] Gersak B, Kiser AC, Bartus K, et al. Importance of evaluating conduction block in radiofrequency ablation for atrial fibrillation. Eur J Cardiothorac Surg 2012 Jan;41(1):113–8.

[38] Pappone C, Santinelli V, Manguso F, et al. Pulmonary vein denervation enhances long-term benefit after circumferential ablation for paroxysmal atrial fibrillation. Circulation 2004;109:327–34.

[39] Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Europace 2010;12:1360–420.

[40] de Groot JR, Driessen AH, Van Boven WJ, et al. Epicardial confirmation of conduction block during thoracoscopic surgery for atrial fibrillation - a hybrid surgical-electrophysiological approach. Minim Invasive Ther Allied Technol 2012 Jul;21(4):293–301.

[41] Zeng Y, Cui Y, Li Y, et al. Recurrent atrial arrhythmia after minimally invasive pulmonary vein isolation for atrial fibrillation. Ann Thorac Surg 2010;90:510–5.

[42] Kron J, Kasirajan V, Wood MA, et al. Management of recurrent atrial arrhythmias after minimally invasive surgical pulmonary vein isolation and ganglionic plexi ablation for atrial fibrillation. Hear Rhythm 2010;7:445–51.